Disorders of the cardiac outflow tract (OFT) comprise the majority of serious congenital heart disease (CHD). Formation of the OFT results from the finely controlled interplay of several cell populations, including cardiac neural crest (CNC), OFT endothelium, and pharyngeal mesoderm (secondary heart field, SHF). In mouse, CNC is required for normal patterning of the OFT, particularly the septation of the OFT into separate systemic and pulmonary outflows. To further understand the role of CNC in OFT patterning, microRNA (miRNA) regulatory function in the CNC was disrupted through *Pax3*-specific deletion of *Dicer*, a critical processor miRNA precursor transcripts to functional miRNAs. Normal miRNA expression is lost in the *Pax3* fate mapped domain, including the dorsal neural tube, neural crest, and presomitic mesoderm. Loss of *Dicer* in the *Pax3* domain leads to midgestational embryonic lethality and a series of patterning defects affecting the branchial arches, hypaxial musculature, and the OFT. In particular, the abnormal patterning of the OFT is reminiscent of serious forms of CHD. This work will describe specific abnormalities in neural crest differentiation and function with the loss of normal miRNAs. In addition, candidate miRNAs and gene targets will be discussed, as well as the impact of these findings for clinical CHD.

doi:10.1016/j.ydbio.2009.05.228

Program/Abstract # 206
Patterning of the developing posterior murine circulatory system
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Although vascular misconnections between the umbilical cord, yolk sac and fetus are associated with a variety of birth defects, how this normal relationship is established is obscure. During elongation, the distal allantois develops a highly branched vasculature that provides a wide vascular surface area for fusion with the chorion. By contrast, the proximal region develops a thick, unbranched vasculature that amalgamates with the embryonic dorsal aorta and yolk sac blood vessels. Using simple methodologies in fixed and living whole mouse embryos, our results suggest that the outer surface of the allantois, together with visceral endoderm, cooperates to establish a vascular continuum within the mammalian conceptus for optimal maternal exchange during gestation.

doi:10.1016/j.ydbio.2009.05.229

Program/Abstract # 207
Endocardial requirements for myocardial morphogenesis
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Organogenesis requires the specification of diverse cell fates, coordinated cellular movements and cellular interactions to generate a properly formed organ. Vertebrate heart formation begins as myocardial precursors move to the midline, where they surround a central endocardial core, to form a cardiac ring that elongates into a linear heart tube. Interactions between these two layers instruct the morphological and physiological properties of both layers during both linear heart tube formation and later cardiac maturation. Because the linear heart tube serves as a scaffold for further cardiac maturation, even small errors in these endocardial/myocardial interactions can have grave consequences on cardiac function. We have demonstrated a requirement for early interactions between the endocardium and myocardium in regulating myocardial cell migration. In addition, we have identified a morphologically distinct flk1 positive, fli-1 negative subpopulation of endocardial cells we call the endocardial ring juxtaposed to the myocardium at cardiac ring stage. Loss of these cells results in the formation of a dismorphic cardiac ring and heart tube defects. We hypothesize that a newly identified VEGF receptor expressing endocardial subpopulation directs the formation of the myocardial ring, a key step in heart tube assembly that acts as a scaffold for myocardial elongation. To test this hypothesis, we are assessing the requirement for VEGFR in formation of endocardial ring and test the requirement for the endocardial ring in directing heart tube assembly by removing distinct endocardial subpopulations using MOs and confocal microscopy to assess myocardial and endocardial cell behavior.

doi:10.1016/j.ydbio.2009.05.230

Program/Abstract # 208
Pro-epicardial and inflow myocardial cells share common lineage in avian
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The heart wall is composed by three different layers: endo-, myo- and epicardium. The origin of the epicardium is traced only to the pro-epicardium, a cauliflower organ that is formed on the right sinus horn of the heart inflow region (sinus venosus) but the progenitor cells of the pro-epicardium organ itself are not known. 3-D reconstruction and early expression of Tbx18 suggested that the progenitor cells of the pro-epicardium organ might be localized in the pre-myocardium of the inflow region. We attempted to fate map the pro-epicardium organ by using live fluorescent labeling in vivo. Fluorescent crystals were inserted in the right and left sinus horn at the somitic level of 912 somite chick embryos and migration and differentiation of labeled cells were followed. The results showed that when crystals inserted in the heart filed, namely the caudal area of the heart inflow around stage HH1011 but only on the right side, the inflow cells contribute to the pro-epicardium organ where the crystal inserted in the left side contributed only to the myocardium. This shows that the pro-epicardial and inflow myocardial cells share common lineage in avian. The pro-epicardium cells then move over the heart surface to form the epicardium layer which contributes to the formation of the coronary vasculature and other structures of the heart.

doi:10.1016/j.ydbio.2009.05.231

Program/Abstract # 209
Wise/Sostdc1 regulates survival and growth of the mouse tooth bud by inhibiting Wnt signaling
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Mammalian tooth develops through the epithelialmesenchymal interactions involving a number of signaling pathways. However, little is known on how the level of each signaling is precisely controlled and how different pathways interact with each other during the processes. In Wise-null mice, multiple aspects of tooth development are disrupted resulting in abnormal tooth number, size and cusp pattern. Here, we show that most of the mutant phenotypes can be rescued by reducing dosage of Wnt co-receptors, LRP5 and LRP6, suggesting direct interaction of Wise with the co-receptors. Our analysis with the TopGal reporter